THE OPTIMAL TEMPERATURE FOR MYOCARDIAL PROTECTION DURING PROLONGED ISCHEMIA AS ASSESSED BY PHOSPHORUS-31 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY (P31-NMR).

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The optimal level of hypothermia during myocardial preservation for cardiac transplantation still needs to be defined. Therefore P31-NMR spectroscopy was applied to assess the effect of different preservation temperatures on time dependant changes of high energy phosphorous compounds in isolated rat hearts during prolonged ischemia and subsequent reperfusion. Hearts were flushed and stored in modified St. Thomas Hospital solution at 15°C for 5 hours (group 1,n=6) or at 4°C for 8 hours (group 2,n=6). Results: Phosphocreatine dropped in both groups within two hours to less than 5µmol/g dry weight (dw). ATP depletion during ischemia was slower in group 2 leading to significant differences between both groups after 3 hours of ischemia (in µmol/g dw: 9.1±0.7 in group 2 vs. 4.6±2.7 in group 1 at 3 hours, $p<0.025$). The intracellular pH dropped at 5 hours of ischemia to 6.16±0.1 in group 1 and 6.71±0.2 in group 2 ($p<0.01$). Hemodynamic recovery after 1 hour of reperfusion was superior in group 2, although the ischemic time was 3 hours longer in this group compared to group 1 (in % of preischemic value): LV-peak systolic pressure: 84±2 vs. 49±6, $p<0.001$; LV+dp/dt max: 81±5 vs. 38±6, $p<0.0025$; rate * pressure product: 74±4 vs. 32±5, $p<0.0025$ and coronary flow: 82±11 vs. 41±3, $p<0.0025$. Conclusion: Hypothermia at 4°C appears favourable for prolonged myocardial protection compared to 15° with regard to preservation of ATP and postischemic hemodynamic function.

TEMPORARY CORONARY STENOSIS ASSOCIATED WITH VENTRICULAR ARRHYTHMIA 24-48 HOURS AFTER REPERFUSION

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Clinical reports indicate the delayed occurrence of sudden cardiac death following stressful events, but mechanisms are not yet understood. Increased study of myocardial and microvascular stunning following ischemia may provide potential models for such mechanisms. To study electrophysiological consequences of temporary reductions in coronary blood flow (CBF), 7 dogs were prepared with aortic catheters to measure mean arterial pressure (MAP), Doppler flow probes to measure circumflex CBF, and RV pacing catheters to determine repetitive extrasystole threshold (RET) (current needed to induce spontaneous ventricular beat), and ECG. MAP, heart rate (HR), CBF, RET and ECG were examined in control before coronary stenosis, during 90 minutes of a 60% reduction in CBF and at 1, 24, 48 and 72 hours after reperfusion. MAP and HR did not vary significantly from control (87±2 mmHg and 104±6 bpm) during stenosis or at 1, 24, 48 hrs after reperfusion. However, frequent ventricular ectopic activity, not present in control or stenosis, was noted at 24-48 hrs. RET was 20±3 ma in control, 19±3 ma during stenosis, decreased significantly to 11±2 ma at 24-48 hrs after reperfusion ($p<0.05$), and was 20±4 ma at 72 hrs. Creatine phosphokinase values doubled at 24-48 hrs ($p<0.05$). These results indicate a predisposition to arrhythmia 24-48 hrs after an episode of acute coronary stenosis, perhaps due to isolated necrosis secondary to transient ischemia, causing a delayed, electrophysiological "stunning".

REDUCTION OF INFARCT SIZE BY PRECONDITIONING ISCHEMIA: A TRANSIENT PHENOMENON ?

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Experimental evidence, primarily from canine studies, suggests that short periods of ischemia "precondition" the heart so that subsequent, longer periods of ischemia cause less necrosis than expected. We tested this concept in a model of low collateral blood flow, chosen because of its similarity with human myocardial blood supply. In addition, we sought to determine whether any protective effect of preconditioning was maintained or was lost over time. We examined 3 groups of rats:

1. Control (C): hearts were subjected to 90 minutes of coronary artery occlusion (CAO) followed by 4.5 hours of reperfusion (n=6).
2. Preconditioning (P): hearts were preconditioned by three, 3-minute periods of CAO, each separated by 5 minutes of reperfusion. This was followed by 90 minutes of CAO and a further period of reperfusion (n=6).
3. Preconditioning + delayed occlusion (P + D): the same regime was used to precondition the hearts; however, the 90 minute CAO was delayed for 2 hours after preconditioning (n=6).

Planimetry was used to measure area at risk (AR) following injection of dye and area of necrosis (AN) after tetrazolium staining. Values are expressed as mean ± SD (* $p < 0.05$ versus control).

	C	P	P + D
AR/LV (%)	43.9±16.4	38.4±17.8	39.8±10.5
AN/AR (%)	60.2±16.0	30.5±21.9*	45.4±13.4

Although all of the groups had a comparable area at risk, we found that preconditioning significantly reduced infarct size versus control. However, it appears that a 2 hour delay between preconditioning and prolonged ischemia removes at least some of the beneficial effects of preconditioning. In conclusion, the positive effects of preconditioning in this low collateral flow model appear to be transient.

BETA-ADRENERGIC ALTERATIONS IN RAT IMMUNE FUNCTION FOLLOWING MYOCARDIAL INFARCTION

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The link between the sympathetic nervous and immune system is controversial. In order to determine whether the changes in sympathetic traffic that is seen during myocardial ischemia are associated with abnormalities in immune responsiveness, we studied the effects of ischemia on beta-adrenergic receptor expression and mitogen proliferation on rat splenocytes. Rats were anesthetized with ketamine/xylazine (3:1), intubated, and ventilated with supplemental oxygen. A left thoracotomy was performed and the distal left main coronary artery was ligated with 6-0 prolene suture. Sham operated rats served as controls. Animals were sacrificed and splenectomized at 15 and 60 minutes. When compared to controls, animals sacrificed 15 minutes post ligation had a 25% decrease in expression of splenic beta-adrenergic receptors. This decrease might be reflected by alterations of cellular subpopulations with different densities of receptors. After 60 minutes of ischemia, beta receptor expression returned to pre-ligation values. Con A stimulated ^3H thymidine incorporation in rat splenocytes undergoing 15 minutes of ischemia was decreased by approximately 25% compared to controls. However, following 60 minutes of ischemia, there was a 30% augmentation in ^3H thymidine incorporation. Thus it appears that ischemia leads to time dependent alteratins in immune responsiveness. These alterations appear in part to be mediated by the beta-adrenergic pathway.